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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/726,546 | 12/04/2003 | Paolo Chiesi | 245855US0CIP | 5501 |

22850 7590 06/15/2007

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| EXAMINER | |
|---|---|
| SAMALA, JAGADISHWAR RAO | |
| **ART UNIT** | **PAPER NUMBER** |
| 1618 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 06/15/2007 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/726,546 | CHIESI ET AL. | |
| | Examiner | Art Unit | |
| | Jagadishwar R. Samala | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 8-34 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 8-34 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 12/04/2003.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**Response to Amendment**

1. The amendment filed on March 27, 2007 has been entered.

Previous rejections that are not reiterated herein are withdrawn.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 8-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chiesi (US 4,826,875 here after '875) in view of Barry et al., (US 5,055,306 here after '306).

Chiesi discloses a pharmaceutical composition as an immediate release of active principles, or may be formulated to allow a planned and sequential release of levodopa methyl ester and carbidopa for the treatment of Parkinson's disease and neuralgic syndromes connected with it (see abstract and column 6, lines 15-40). And also discloses a single oral dosage data of the levodopa methyl ester plasmatic levels at the different times after administration, reaching the maximum plasma concentration peak of levodopa at 0.31 minutes from the administration (i.e., the rapid attainment of high concentrations of levodopa in the systemic circulations after levodopa methyl ester administration produces a very early onset of the therapeutic effect, which appears at 20-30 minutes about from the administration of the composition, see column 5, lines 32-65)

Chiesi fails to disclose pharmaceutical composition wherein additional acid-base couples such as sodium glycine carbonate and fumaric acid capable of reacting rapidly with base, an effervescent action occurs as the carbon dioxide gas is desorbed from the inorganic oxide material. However the use of sodium glycine carbonate and fumaric acid as an effervescent acid-base couple, suitable for dissolving in water or an aqueous solution is well known in the art as shown by Barry et al.

Barry discloses a granular sustained-release formulation of a pharmacologically active substance such as levodopa in the form of a tablet comprising a predetermined dose or number of doses of the pharmacologically active substance and effervescent acid-base couple, because the addition of sodium glycine carbonate and fumaric acid provides the effervescent and exothermic reaction when mixed with water to enhance release of a therapeutic agent or water-dispersible ingredients (see column 3, lines 35-44). And also the composition provides sustained-release formulations, which enable large dosages to be more easily administered to, and swallowed by, the patient.

It would have been obvious to one of ordinary skill in the art to modify the pharmaceutical composition disclosed by Chiesi to include sodium glycine carbonate-fumaric acid as an effervescent acid-base couple as an additional effervescent compositions as a means of administering solubilized therapeutic agents. Various effervescent compositions are known which have exothermic heats of solution. A number of these are listed in Lange's Handbook of Chemistry, 11$^{th}$ edition, in table 9-6 (page 9-107) and a review of such tablets appears in The Pharmaceutical Journal, Mar. 12, 1983, p289-294, (F.E.J. Sendall et al.). The greater the value of the heat of solution, the more heat is liberated per gram-mole of the substance. One of ordinary

skill in the art would have been motivated to include the sodium glycine carbonate-fumaric acid as an effervescent acid-base couple as an additional effervescent compositions in the pharmaceutical composition disclosed by Chiesi because the effervescent acid-base couple taught by Barry, while having a similar therapeutic effectiveness of pharmaceutical composition, provides an additional and effervescent advantage of solubilizing therapeutic agents as compared to the pharmaceutical composition disclosed by Chiesi. Utilizing this combination of materials promotes and enhances release of the therapeutic agents beyond that achievable by using either other pharmaceutically acceptable components alone.

**Response to Arguments**

2. Applicant's arguments with respect to rejection of claims 8-34 under 103(a) have been fully considered but they are not persuasive. It remains the position of the primary reference patent by the process of secondary reference patent since combined together both patents discloses pharmaceutical composition for the treatment of Parkinson's disease, containing as the active principle levodopa methyl ester combined with carbidopa in the form of a effervescent tablet.

Applicant asserts that Barry et al. composition, containing the active ingredient would lead to controlled /retarded release of the active ingredient.

This is not found persuasive because Barry does discloses the pharmaceutical composition that provides sustained-release formulations and can be designed to delver specific doses of a particular pharmacologically active substance over a predetermined period of time

(see column 7, lines 64-68). And also, the composition disclosed by Baary enables large dosages in sustained-release form to be more easily administered to, and swallowed by, the patient.

Applicant asserts that Chiesi composition showed slow absorption and an active ingredient lesser exposure during the first hours after administration.

This is not found persuasive because Chiesi does discloses the composition administering sublingual way provides effective and grants remarkable advantages: more rapid and reliable absorption than from the gastrointestinal tract and when administration is the buccal delivery by small tablets which adhere to the surface to the oral mucosa releasing drug amount constant in time, assuring steady plasmatic levels at the different times after administration respectively.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

*Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 8, 10-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim1 of U.S. Patent No. 6,284,272. Although the conflicting claims are not identical, they are not patentably distinct from each other because each are drawn to a pharmaceutical composition comprising active ingredient is a combination of levodopa methyl ester and carbidopa and an effervescent acid-base couple containing fumaric acid-sodium glycine carbonate, wherein administering a single oral dose of said composition to a human with only slightly differences in describing the functionalities of the components. For the most part, the patented claims are within the scope of the instant claims. Claim 1 is generic to all that is recited in claim 1 of US patent 6,284,272. That is, claim 1 falls entirely within the scope of claim 1 of the patent, or is anticipated thereby. Further both pharmaceutical compositions require active ingredients levodopa methyl ester and carbidopa and an effervescent components in the same proportions or identical. If issued the "272 patent claims would act as obviating art over the instant claims.

***Conclusion***

1. No claims are allowed at this time.

2. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE MONTH shortened statutory period, then the, shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jagadishwar R. Samala whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jagadishwar R Samala
Examiner
Art Unit 1618

sjr

MICHAEL G. HARTLEY
SUPERVISOR
SPE